AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for selecting ~~or designing~~ a compound for modulating the activity of phosphoinositide dependent protein kinase 1 (PDK1), the method comprising:

~~the step of using molecular~~ modelling ~~means to select or design a compound that is predicted to interact with the protein kinase catalytic domain of PDK1, wherein~~ a three-dimensional structure of a plurality of molecules in a computer;

comparing a three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 ~~is compared~~ with ~~a~~ the three-dimensional structure of ~~a compound~~ each of said molecules[[,]]; and,

selecting ~~a compound that is predicted~~ said compound as one of the modelled molecules based on a predicted ability of the molecule to interact with ~~the~~ said protein kinase catalytic domain ~~is selected~~, wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 is a three-dimensional structure ~~(~~or part thereof~~)~~ determined for a polypeptide ~~consisting of~~ comprising residues equivalent to residues 51 to 359 of full length human PDK1 (SEQ ID NO. 3), or a fragment or fusion thereof.

2. (Currently Amended) The method of claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is a three-dimensional structure ~~(~~or part thereof~~)~~ determined for a polypeptide consisting of residues 51 to 359 of full length human PDK1 (SEQ ID NO. 3) or a fusion thereof.

3. (Currently Amended) The method of claim 2 wherein the three-dimensional structure ~~(~~or part thereof~~)~~ is determined for a polypeptide consisting of residues 51 to 359 of full length human PDK1 (SEQ ID NO. 3) and the amino acid sequence Gly-Pro preceding the methionine corresponding to Met51 of human PDK1.

4. (Currently Amended) The method of claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is a three-dimensional structure ~~(~~or part thereof~~)~~ determined for a polypeptide consisting of residues 71 to 359 of full length human PDK1 (SEQ ID NO. 3) or a fusion thereof.

5. (Currently amended) The method of claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is obtainable by X-ray analysis of a crystal obtainable using a mother liquor solution comprising ammonium sulphate.

6. (Original) The method of claim 5 wherein the mother liquor solution is of pH 7 to 9.

7. (Original) The method of claim 6 wherein the mother liquor solution is of pH 8.5.

8. (Previously presented) The method of claim 7 wherein the mother liquor solution comprises ATP.

9. (Currently Amended) The method of claim 1 wherein the three-dimensional structure of at least a part of the protein kinase catalytic domain of PDK1 structure is that represented by the structure co-ordinates shown in Examples 2, 3, ~~or~~ 4, ~~or~~ 7 or 8, or a structure modelled on such structure co-ordinates.

10. (Currently Amended) The method of claim 1 wherein the molecule is predicted to bind to a region of the structure termed the "PIF binding pocket" ~~(~~formed by residues including residues Lys115, Ile118, Ile119 on the αB helix, Val124, Val127 on the αC helix and Leu 155 on β-sheet 5 of full length human PDK1 (SEQ ID NO. 3), or equivalent residues~~)~~, the "phosphate binding pocket" ~~(~~formed by residues including residues Lys76, Arg 131, Thr 148 and Gln150 of full length human PDK1 (SEQ ID NO. 3), or equivalent residues~~)~~ and/or the αC helix ~~(~~ formed by residues equivalent to 123-136 of full length human PDK1 (SEQ ID NO. 3)~~)~~, or interacting regions.

11. (Currently Amended) The method of claim 1 wherein the compound is for modulating the protein kinase activity of PDK1 towards protein kinase B (PKB) or other pleckstrin homology (PH)-domain-comprising/phosphoinositide-binding substrate of PDK1.

12. (Currently Amended) The method of claim 1 wherein the compound is for modulating the protein kinase activity of PDK1 towards serum and glucocorticoid stimulated protein kinase (SGK), S6 kinase (S6K) or other substrate of PDK1 whose phosphorylation by PDK1 is promoted by phosphorylation of the substrate on the Ser/Thr of the "hydrophobic motif" FXXFS/TY (SEQ ID NO. 2).

13. (Currently Amended) A method for selecting ~~or designing~~ a compound for modulating the activity of a ~~hydrophobic pocket (~~PDK1 Interacting Fragment (PIF) binding pocket~~)~~-containing protein kinase having ~~a~~ said ~~hydrophobic pocket~~ PIF binding pocket in the position

equivalent to ~~the~~ a hydrophobic pocket of human PDK1 that is defined by residues including Lys115, Ile118, Ile119, Val124, Val127 and/or Leu155 of full-length human PDK1 (SEQ ID NO. 3) and further having a phosphate binding pocket in the position equivalent to the phosphate binding pocket of human PDK1 that is defined by residues including Lys76, Arg131, Thr148 and/or Gln150 of SEQ ID NO. 3, the method comprising:

~~the step of using molecular~~ modelling ~~means to select or design a compound that is predicted to interact with the said hydrophobic pocket-containing protein kinase, wherein~~ a three-dimensional structure of a plurality of molecules in a computer;

comparing ~~a~~ the three-dimensional structure of ~~a compound~~ each of said molecules ~~is compared~~ with ~~a~~ the three-dimensional structure of ~~the~~ said phosphate binding pocket and optionally also ~~the~~ said hydrophobic pocket and/or αC helix or region interacting therewith;[[,]] and,

selecting ~~a~~ said compound as one of the modelled molecules ~~that is predicted~~ based on a predicted ability of the molecule to interact with ~~the~~ said phosphate binding pocket and optionally also ~~the~~ said hydrophobic pocket and/or αC helix or region interacting therewith, ~~is selected~~.

14. (Withdrawn) The method of claim 13 wherein the protein kinase is an isoform of Serum and Glucocorticoid stimulated protein kinase (SGK), Protein Kinase B (PKB), p70 S6 kinase, p90 RSK, PKC isoforms (for example PKCα, PKCδ, PKCζ), PRK1, PRK2, MSK1 or MSK2.

15. (Previously presented) The method of claim 13 wherein the three-dimensional structure of said phosphate binding pocket and optionally also the hydrophobic pocket and/or αC helix or region interacting therewith is a structure modelled on the basis of a three-dimensional structure as defined in claim 9.

16. (Previously presented) The method of claim 1 further comprising the step of synthesising, purifying and/or formulating the compound.

17-42. (Canceled)

43. (New) The method of claim 1, wherein the method further comprises:

designing one or more of said molecules prior modelling.

44. (New) The method of claim 13, wherein the method further comprises:

designing one or more of said molecules prior modelling.